

CLAIMS

What is claimed is:

1. An isolated nucleic acid comprising:
a nucleic acid encoding a protein disulfide isomerase protein selected from the group consisting of:
 - a) a protein disulfide isomerase comprising an amino acid sequence as set forth in SEQ ID NO:2;
 - b) a protein disulfide isomerase comprising an amino acid sequence as set forth in SEQ ID NO:4;
 - c) a protein disulfide isomerase comprising an amino acid sequence as set forth in SEQ ID NO:6;
 - d) a protein disulfide isomerase comprising an amino acid sequence as set forth in SEQ ID NO:8;
 - e) a protein disulfide isomerase having at least 57% identity to a protein disulfide isomerase selected from the group consisting of SEQ ID NO: 2, SEQ ID NO:4, SEQ ID NO:6, and SEQ ID NO:8, having protein disulfide isomerase activity; and
 - f) a fragment of said protein disulfide isomerase of (a), (b), (c), (d) or (e), wherein said fragment encodes a protein having protein disulfide isomerase activity.
2. The isolated nucleic acid of claim 1, wherein said isolated nucleic acid is selected from the group consisting of a nucleotide sequence as set forth in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, and SEQ ID NO:7.
3. The isolated nucleic acid of claim 1, further comprising vector sequences.

4. The isolated nucleic acid of claim 3, wherein said vector is an expression vector.
5. The isolated nucleic acid of claim 1, wherein said isolated nucleic acid is from a member of the genus *Conus*.
6. A host cell comprising a cell containing the vector of claim 3.
7. A host cell comprising a cell containing the vector of claim 4.
8. The host cells of claim 7, further comprising an expression vector encoding a disulfide-rich peptide, wherein said expression vector encoding a disulfide-rich peptide and said expression vector encoding a protein disulfide isomerase comprise one or more nucleic acid molecules.
9. A method for producing a protein disulfide isomerase comprising:
introducing into a host cell a nucleic acid encoding protein disulfide isomerase selected from the group consisting of:
 - a) a protein disulfide isomerase comprising an amino acid sequence as set forth in SEQ ID NO:2;
 - b) a protein disulfide isomerase comprising an amino acid sequence as set forth in SEQ ID NO:4;
 - c) a protein disulfide isomerase comprising an amino acid sequence as set forth in SEQ ID NO:6;
 - d) a protein disulfide isomerase comprising an amino acid sequence as set forth in SEQ ID NO:8;
 - e) a protein disulfide isomerase having at least 57% identity to a protein disulfide isomerase selected from the group consisting of SEQ ID NO:2, SEQ

ID NO:4, SEQ ID NO:6, and SEQ ID NO:8, having protein disulfide isomerase activity; and

- f) a fragment of said protein disulfide isomerase of (a), (b), (c), (d) or (e), wherein said fragment encodes a protein having protein disulfide isomerase activity;

expressing said protein disulfide isomerase; and

isolating said protein disulfide isomerase.

10. The method according to claim 9, wherein said cell is selected from the group consisting of an insect cell, HIGH FIVE™, Sf9, Sf21, *Drosophila* Schneider2, a mammalian cell, COS 1, NIH 3T3, HeLa, 293, CHO, U266, a plant cells, Baculovirus, *Saccharomyces*, *Schizosaccharomyces*, *Aspergillus*, *E. coli*, and *Bacillus*.

11. A method for producing a correctly-folded disulfide-rich peptide comprising:
introducing a nucleic acid encoding a protein disulfide isomerase and a nucleic acid encoding a disulfide-rich peptide into a host cell, wherein said nucleic acid encoding a protein disulfide isomerase and a disulfide-rich peptide comprise one or more nucleic acid molecules;

expressing a protein disulfide isomerase peptide and a disulfide-rich peptide, wherein said disulfide-rich peptide is a conotoxin; and

isolating a correctly-folded disulfide-rich peptide.

12. The method according to claim 11, wherein said host cell is selected from the group consisting of an insect cell, HIGH FIVE™, Sf9, Sf21, *Drosophila* Schneider2, a mammalian cell, COS 1, NIH 3T3, HeLa, 293, CHO, U266, a plant cells, Baculovirus, *Saccharomyces*, *Schizosaccharomyces*, *Aspergillus*, *E. coli*, and *Bacillus*.

13. The method according to claim 11, wherein said protein disulfide isomerase peptide is from a member of the genus *Conus*.

14. A method for producing a correctly-folded disulfide-rich peptide comprising:
introducing into a host cell a nucleic acid encoding a protein disulfide isomerase selected from the group consisting of:

- a) a protein disulfide isomerase comprising an amino acid sequence as set forth in SEQ ID NO:2;
- b) a protein disulfide isomerase comprising an amino acid sequence as set forth in SEQ ID NO:4;
- c) a protein disulfide isomerase comprising an amino acid sequence as set forth in SEQ ID NO:6;
- d) a protein disulfide isomerase comprising an amino acid sequence as set forth in SEQ ID NO:8;
- e) a protein disulfide isomerase having at least 57% identity to a protein disulfide isomerase selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, and SEQ ID NO:8, having protein disulfide isomerase activity; and
- f) a fragment of said protein disulfide isomerase of (a), (b), (c), (d) or (e), wherein said fragment encodes a protein having protein disulfide isomerase activity

introducing a nucleic acid encoding a disulfide-rich peptide, wherein said nucleic acid encoding a protein disulfide isomerase and said nucleic acid encoding a disulfide-rich peptide comprise one or more nucleic acid molecules;

expressing a protein disulfide isomerase peptide and a disulfide-rich peptide; and
isolating a correctly-folded disulfide-rich peptide.

15. The method according to claim 14, wherein said cell is selected from the group consisting of an insect cell, HIGH FIVE™, Sf9, Sf21, *Drosophila Schneider*2, a mammalian cell, COS 1, NIH 3T3, HeLa, 293, CHO, U266, a plant cells, Baculovirus, *Saccharomyces*, *Schizosaccharomyces*, *Aspergillus*, *E. coli*, and *Bacillus*.

16. The method according to claim 14, wherein said disulfide-rich peptide is a conotoxin.

17. An isolated protein disulfide isomerase polypeptide comprising a protein disulfide isomerase selected from the group consisting of an amino acid sequence as set forth in SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, a protein having at least 57% identity to said protein disulfide isomerase and a fragment thereof, wherein said protein disulfide isomerase or fragment thereof has protein disulfide isomerase activity.

18. A method for producing a correctly-folded disulfide-rich peptide comprising:
combining a disulfide-rich peptide and a protein disulfide isomerase, wherein said protein disulfide isomerase is selected from the group consisting of a protein disulfide isomerase as set forth in SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, a protein having at least 57% identity to said protein disulfide isomerase and a fragment thereof, wherein said protein disulfide isomerase or fragment thereof has protein disulfide isomerase activity; and
isolating said correctly-folded disulfide-rich peptide.

19. The method according to claim 18, wherein said disulfide-rich peptide is a conotoxin polypeptide.

20. The method according to claim 18, further comprising:
adding a cell extract.

21. The method according to claim 20, wherein said cell extract comprises a translation system.
22. The method according to claim 21, wherein said cell extract further comprising a transcription system.
23. A method for producing a correctly-folded disulfide-rich peptide comprising:
combining a disulfide-rich conotoxin peptide and a protein disulfide isomerase or fragment thereof, wherein said fragment has protein disulfide isomerase activity; and
isolating said correctly-folded disulfide-rich peptide.
24. The method according to claim 23, further comprising:
adding a cell extract.
25. The method according to claim 24, wherein said cell extract comprises a translation system.
26. The method according to claim 25, wherein said cell extract further comprising a transcription system.
27. The method according to claim 23, wherein said protein disulfide isomerase is from a member of the genus *Conus*.